IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: BONFANTI, Jean-François et al.

Serial No.: Not Assigned Art Unit: TBA

Filed: Herewith

For : PIPERIDINE-AMINO-BENZIMIDAZOLE DERIVATIVES AS INHIBITORS OF RESPIRATORY SYNCYTIAL VIRUS REPLICATION

Mail Stop: PCT
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT "A"

Dear Sir:

Prior to examination and calculation of fees due, please amend the above-identified application as follows.

☒ Amendments to the Specification begin on page 2 of this paper.

☒ Amendments to the Claims are reflected in the listing of the claims which begins on page 3 of this paper.

☐ Amendments to the Drawings begin on page of this paper and include an attached replacement sheet.

☒ Remarks begin on page 10 of this paper.

AMENDMENTS TO SPECIFICATION

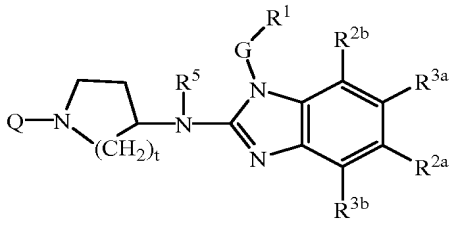
Page 1, between the Title and line 4, please insert the following new paragraph:

--Cross Reference to Related Applications

This application is the national stage of PCT Application No. PCT/EP2004/053606, filed December 20, 2004, which application claims priority from European Patent Application No. 03104802.8, filed 18 December 2003 and US provisional Patent Application No. 60/566835, filed 30 April 2004, the entire disclosures of which are hereby incorporated in their entirely.--

Listing of Claims

1. (Original) A compound of formula (I)



(I)

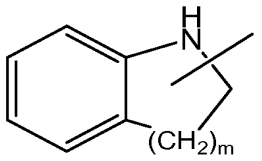
a prodrug, *N*-oxide, addition salt, quaternary amine, metal complex or stereochemically isomeric form thereof wherein

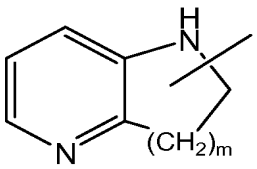
Q is C_{1-6}alkyl optionally substituted with one or more substituents each independently selected from the group consisting of trifluoromethyl, C_{3-7}cycloalkyl, Ar^2, hydroxy, C_{1-4}alkoxy, C_{1-4}alkylthio, Ar^2-oxy-, Ar^2-thio-, $Ar^2(CH_2)_n$oxy, $Ar^2(CH_2)_n$thio, hydroxycarbonyl, aminocarbonyl, C_{1-4}alkylcarbonyl, Ar^2carbonyl, C_{1-4}alkoxycarbonyl, $Ar^2(CH_2)_n$carbonyl, aminocarbonyloxy, C_{1-4}alkylcarbonyl-oxy, Ar^2carbonyloxy, $Ar^2(CH_2)_n$carbonyloxy, C_{1-4}alkoxycarbonyl$(CH_2)_n$oxy, mono- or di(C_{1-4}alkyl)aminocarbonyl, mono- or di(C_{1-4}alkyl)aminocarbonyloxy, aminosulfonyl, mono- or di(C_{1-4}alkyl)aminosulfonyl or a heterocycle selected from the group consisting of pyrrolidinyl, pyrrolyl, dihydropyrrolyl, imidazolyl, triazolyl, piperidinyl, homopiperidinyl, piperazinyl, pyridyl and tetrahydro-pyridyl, wherein each of said heterocycle may optionally be substituted with oxo or C_{1-6}alkyl; or Q is C_{1-6}alkyl substituted with two substituents wherein one substituent is selected from the group consisting of amino, mono- and diC_{1-4}alkyl-amino and Ar^2-C_{1-4}alkylamino and the other substituent is selected from the group consisting of carboxyl, C_{1-6}alkyloxycarbonyl, Ar^2-C_{1-4}alkyloxycarbonyl, aminocarbonyl and aminosulfonyl;

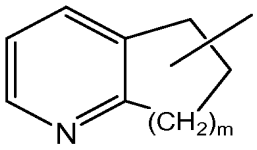
G is a direct bond or C_{1-10}alkanediyl optionally substituted with one or more substituents independently selected from the group consisting of hydroxy, C_{1-6}alkyloxy, Ar^1C_{1-6}alkyloxy, C_{1-6}alkylthio, Ar^1C_{1-6}alkylthio, $HO(-CH_2-CH_2-O)_n$-, C_{1-6}alkyloxy$(-CH_2-CH_2-O)_n$- and Ar^1C_{1-6}alkyloxy$(-CH_2-CH_2-O)_n$-;

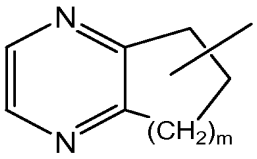
R^1 is Ar^1 or a monocyclic or bicyclic heterocycle being selected from piperidinyl, piperazinyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, furanyl, tetrahydro-furanyl, thienyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl, isothiazolyl, pyrazolyl, isoxazolyl, oxadiazolyl, quinolinyl, quinoxalinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, pyridopyridyl, naphthiridinyl,

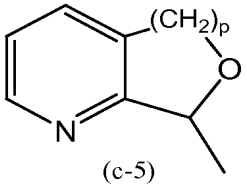
1*H*-imidazo[4,5-b]pyridinyl, 3*H*-imidazo[4,5-b]pyridinyl, imidazo[1,2-a]-pyridinyl, 2,3-dihydro-1,4-dioxino[2,3-b]pyridyl or a radical of formula

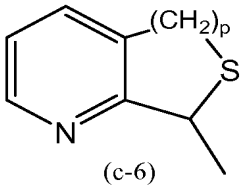

(c-1)

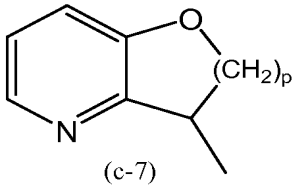

(c-2)

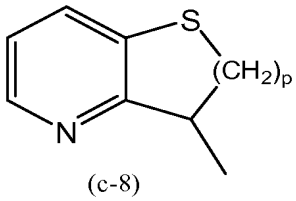

(c-3)


(c-4)


(c-5)


(c-6)


(c-7)


(c-8)

;

wherein each of said monocyclic or bicyclic heterocycles may optionally be substituted with 1 or where possible more, such as 2, 3, 4 or 5, substituents individually selected from the group of substituents consisting of halo, hydroxy, amino, cyano, carboxyl, C_{1-6}alkyl, C_{1-6}alkyloxy, C_{1-6}alkylthio, C_{1-6}alkyloxyC_{1-6}alkyl, Ar^1, Ar^1C_{1-6}alkyl, Ar^1C_{1-6}alkyloxy, hydroxyC_{1-6}alkyl, mono-or di(C_{1-6}alkyl)amino, mono-or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, polyhaloC_{1-6}alkyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkyl-SO_2-NR^{4a}-, Ar^1-SO_2-NR^{4a}-, C_{1-6}alkyloxycarbonyl, -C(=O)-$NR^{4a}R^{4b}$, HO(-CH_2-CH_2-O)$_n$-, halo(-CH_2-CH_2-O)$_n$-, C_{1-6}alkyloxy(-CH_2-CH_2-O)$_n$-, Ar^1C_{1-6}alkyloxy(-CH_2-CH_2-O)$_n$- and mono-or di(C_{1-6}alkyl)amino(-CH_2-CH_2-O)$_n$-;

each n independently is 1, 2, 3 or 4;

one of R^{2a} and R^{3a} is C_{1-6}alkyl and the other one of R^{2a} and R^{3a} is hydrogen;

in case R^{2a} is different from hydrogen then R^{2b} is hydrogen or C_{1-6}alkyl, and R^{3b} is hydrogen;

in case R^{3a} is different from hydrogen then R^{3b} is hydrogen or C_{1-6}alkyl, and R^{2b} is hydrogen; or

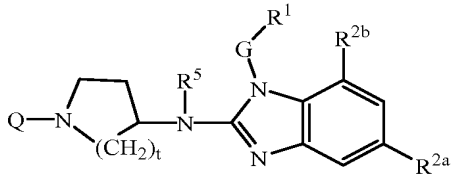
R^{3b} is C_{1-6}alkyl; and R^{3a}, R^{2a}, R^{2b} all are hydrogen; or

R^{2b} is C_{1-6}alkyl; and R^{3a}, R^{2a}, R^{3b} all are hydrogen;

R^{4a} and R^{4b} can be the same or can be different relative to one another, and are each independently hydrogen or C_{1-6}alkyl; or

R^{4a} and R^{4b} taken together may form a bivalent radical of formula $-(CH_2)_s-$;
R^5 is hydrogen or C_{1-6}alkyl;
m is 1 or 2;
p is 1 or 2;
s is 4 or 5;
t is 1, 2 or 3;
Ar^1 is phenyl or phenyl substituted with 1 or more, such as 2, 3 or 4, substituents selected from halo, hydroxy, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, polyhaloC_{1-6}alkyl, and C_{1-6}alkyloxy;
Ar^2 is phenyl or phenyl substituted with 1 or more, such as 2, 3 or 4, substituents selected from the group consisting of halo, hydroxy, amino, cyano, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, polyhaloC_{1-6}alkyl, aminoC_{1-6}alkyl, C_{1-6}alkyloxy, aminosulfonyl, aminocarbonyl, hydroxycarbonyl, C_{1-4}alkylcarbonyl, mono- or di(C_{1-4}alkyl)amino, mono- or di(C_{1-4}alkyl)aminocarbonyl, mono- or di(C_{1-4}alkyl)aminosulfonyl, mono- or di(C_{1-4}alkyl)aminoC_{1-6}alkyl and C_{1-4}alkoxycarbonyl.

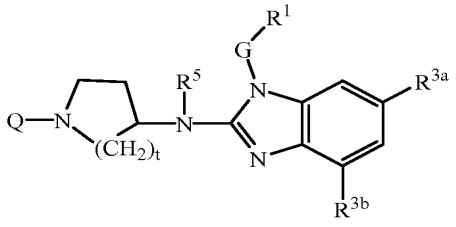
2. (Original) A compound as claimed in claim 1, wherein the compound has the formula



(I-a)

wherein Q, t, R^5, G and R^1 are as claimed in claim 1; and
R^{2a} is C_{1-6}alkyl;
R^{2b} is hydrogen or C_{1-6}alkyl.

3. (Original) A compound as claimed in claim 1, wherein the compound has the formula

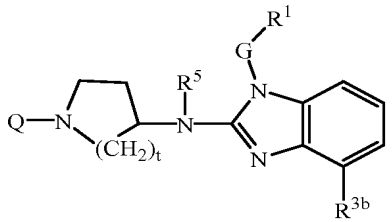


(I-b)

wherein Q, t, R^5, G and R^1 are as claimed in claim 1; and
R^{3a} is C_{1-6}alkyl;

R^{3b} is hydrogen or C_{1-6}alkyl.

4. (Original) A compound as claimed in claim 1, wherein the compound has the formula



(I-c)

wherein Q, t, R^5, G and R^1 are as claimed in claim 1; and
R^{3b} is C_{1-6}alkyl.

5. (Currently Amended) A compound as claimed in claim 1~~any of claims 1 to 4~~ wherein t is 2.

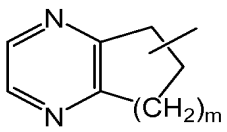
6. (Currently Amended) A compound as claimed in claim 1~~any of claims 1 to 5~~ wherein G is C_{1-10}alkanediyl.

7. (Currently Amended) A compound according to claim 1~~in any of claims 1 – 5~~, wherein G is methylene.

8. (Currently Amended) A compound according to claim 1~~any of claims 1 – 7~~, wherein R^1 is pyridyl optionally substituted with 1 or 2 substituents independently selected from the group consisting of halo, hydroxy, amino, cyano, carboxyl, C_{1-6}alkyl, C_{1-6}alkyloxy, C_{1-6}alkylthio, C_{1-6}alkyloxyC_{1-6}alkyl, Ar^1, Ar^1C_{1-6}alkyl, Ar^1C_{1-6}alkyloxy, hydroxyC_{1-6}alkyl, mono-or di(C_{1-6}alkyl)amino, mono-or di(C_{1-6}alkyl)aminoC_{1-6}alkyl, polyhaloC_{1-6}alkyl, C_{1-6}alkylcarbonylamino, C_{1-6}alkyl-SO_2-NR^{4a}-, Ar^1-SO_2-NR^{4a}-, C_{1-6}alkyloxycarbonyl, -C(=O)-$NR^{4a}R^{4b}$, HO(-CH_2-CH_2-O)$_n$-, halo(-CH_2-CH_2-O)$_n$-, C_{1-6}alkyloxy(-CH_2-CH_2-O)$_n$-, Ar^1C_{1-6}alkyloxy(-CH_2-CH_2-O)$_n$- and mono-or di(C_{1-6}alkyl)amino(-CH_2-CH_2-O)$_n$-.

9. (Currently Amended) A compound according to claim 1~~any of claims 1 – 7~~, wherein R^1 is pyridyl substituted with 1 or 2 substituents independently selected from the group consisting of hydroxy and C_{1-6}alkyl.

10. (Currently Amended) A compound according to claim 1~~any of claims 1 – 7~~, wherein R^1 is Ar^1, quinolinyl, benzimidazolyl, a radical of formula



(c-4)

or pyrazinyl; wherein each of the radicals Ar^1, quinolinyl, benzimidazolyl, (c-4), or pyrazinyl may optionally be substituted with the substitutents of said radicals as claimed in claim1.

11. (Currently Amended) A compound according to claim 1~~any of claims 1 – 7~~, wherein R^1 is phenyl optionally substituted with one, two or three radicals selected from the group consisting of halo, hydroxy, C_{1-6}alkyl, C_{1-6}alkyloxy; quinolinyl; a radical (c-4) wherein m is 2, optionally substituted with up to two radicals selected from C_{1-6}alkyl; benzimidazolyl optionally substituted with C_{1-6}alkyl; pyrazinyl optionally substituted with up to three radicals selected from C_{1-6}alkyl.

12. (Currently Amended) A compound according to claim1~~any of claims 1 – 11~~, wherein R^5 is hydrogen.

13. (Currently Amended) A compound according to claim 1~~any of claims 1 – 12~~, wherein Q is C_{1-6}alkyl optionally substituted with one or two substituents each independently selected from trifluoromethyl, C_{3-7}cycloalkyl, Ar^2, hydroxy, C_{1-4}alkoxy, Ar^2-oxy-, $Ar^2(CH_2)_n$oxy, hydroxycarbonyl, aminocarbonyl, C_{1-4}alkylcarbonyl, C_{1-4}alkoxycarbonyl, aminocarbonyloxy, $Ar^2(CH_2)_n$carbonyloxy, C_{1-4}alkoxycarbonyl$(CH_2)_n$oxy, mono- or di(C_{1-4}alkyl)aminocarbonyl, aminosulfonyl, mono- or di(C_{1-4}alkyl)aminosulfonyl or a heterocycle selected from pyrrolidinyl, pyrrolyl, dihydropyrrolyl, imidazolyl, triazolyl, piperidinyl, homopiperidinyl, piperazinyl and tetrahydropyridyl, wherein each of said heterocycle may optionally be substituted with oxo or C_{1-6}alkyl; or Q is C_{1-6}alkyl substituted with two substituents wherein one substituent is selected from amino and the other substituent is selected from carboxyl and C_{1-6}alkyloxycarbonyl;

14. (Currently Amended) A compound according to claim 1~~any of claims 1 – 12~~, wherein Q is C_{1-6}alkyl optionally substituted with one or two substituents each independently selected from aminocarbonyl, C_{1-4}alkoxycarbonyl, aminocarbonyloxy, $Ar^2(CH_2)_n$carbonyloxy, mono- or di(C_{1-4}alkyl)aminocarbonyl, aminosulfonyl, mono- or di(C_{1-4}alkyl)aminosulfonyl, pyrrolidinyl, dihydropyrrolyl, piperidinyl, homopiperidinyl and tetrahydropyridyl; or Q is C_{1-}

$_{6}$alkyl substituted with two substituents wherein one substituent is amino and the other substituent is selected from carboxyl and C_{1-6}alkyloxycarbonyl.

15. (Currently Amended) A compound according to claim 1~~any of claims 1 - 12~~, wherein Q is C_{1-6}alkyl optionally substituted with one substituent selected from aminocarbonyl, C_{1-4}alkoxycarbonyl, aminocarbonyloxy, $Ar^2(CH_2)_n$carbonyloxy, mono- or di(C_{1-4}alkyl)aminocarbonyl, aminosulfonyl, mono- or di(C_{1-4}alkyl)aminosulfonyl, pyrrolidinyl, dihydropyrrolyl, piperidinyl, homopiperidinyl and tetrahydropyridyl, and optionally with a second substituent which is hydroxy or Q is C_{1-6}alkyl substituted with two substituents wherein one substituent is amino and the other substituent is selected from carboxyl and C_{1-6}alkyloxycarbonyl.

16. (Currently Amended) A compound according to claim 1~~any of claims 1 - 12~~, wherein Q is C_{1-6}alkyl substituted with aminocarbonyl, C_{1-4}alkoxycarbonyl, aminocarbonyloxy, mono- or di(C_{1-4}alkyl)aminocarbonyl, aminosulfonyl, mono- or di(C_{1-4}alkyl)aminosulfonyl, pyrrolidinyl, dihydropyrrolyl, piperidinyl, homopiperidinyl or tetrahydropyridyl.

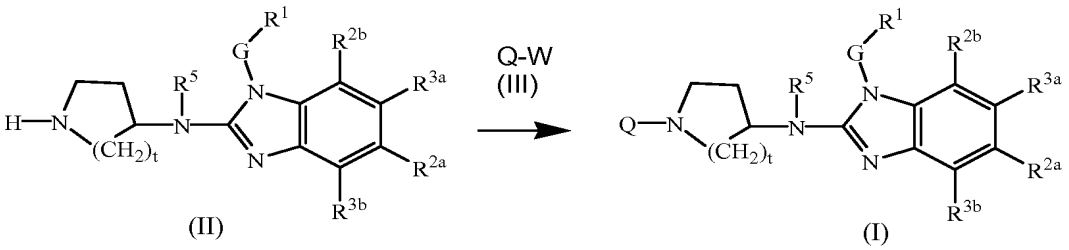
17. (Cancelled)

18. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as claimed in claim 1~~any one of claims 1 to 16~~.

19-20. (Cancelled)

21. (Currently Amended) A process for preparing a compound as claimed in claim 1~~any of claims 1 to 23~~, said process comprising

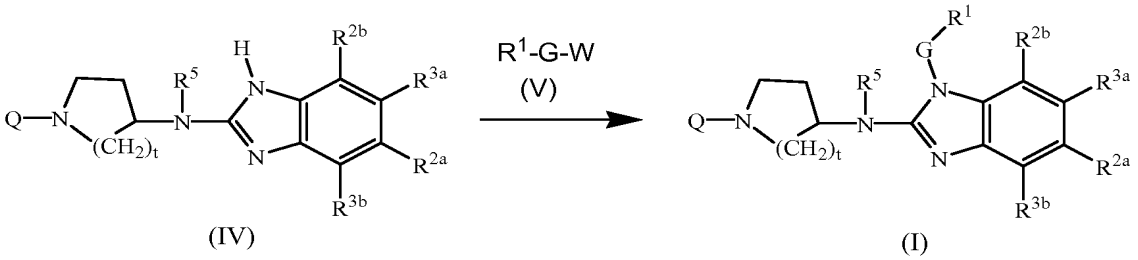
(a) reacting an intermediate of formula (II) with a reagent (III) as in the following reaction scheme:



(II) (I)

(b) reacting an intermediate of formula (IV) with a reagent (V) as in the following

reaction scheme:



(IV) (I)

wherein Q, G, t, R^1, R^{2a}, R^{2b} , R^{3a} , R^{3b}, R^5 are as claimed in claim 1~~any of claims 1 to 16~~; and optionally converting the thus obtained compounds of formula (I) into their pharmaceutically acceptable base-addition or acid addition salt form by treatment with a suitable base or acid and conversely treating the base-addition or acid addition salt form with an acid or a base to obtain the free form of the compound of formula (I).

REMARKS

Consideration of the captioned application in view of the foregoing amendments and following remarks is requested.

The specification has been amended to refer to the priority applications.

Claims 1-16, 18 and 21 are currently pending. Claims 17, 19 and 20 are hereby cancelled and claims 5-16, 18 and 21 are currently amended, without disclaimer of or prejudice to the subject matter deleted therein. No new matter has been added.

Accordingly, the claims pending and under consideration are claims 1-16, 18 and 21.

Early favourable action on the merits is respectfully requested.

Applicant respectfully requests that a timely Notice of Allowance of claims 1-16, 18 and 21 be issued in this case.

Respectfully submitted,

/Alana G. Kriegsman/

By:_____
Alana Kriegsman, Reg. 41,747

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-1495
Dated: June 15, 2006